REMARKS

I. Claim amendments and addition

Claims 1-57 are currently pending. Claims 52-57 have been added and Claims 13-51 have been withdrawn by the Examiner from consideration. Support for amendments to Claim 1 are found throughout the specification and in particular, support for amended Claim 1 is found in the specification at page 3, lines 1 to 3, page 5, lines 15-19, page 5, lines 25 to 32, and page 16, line 15-19. Support for newly added claims is found throughout the specification. In addition, support for Claims 52 and 53 is found at page 9, lines 2 to 4; support for Claim 54 is found at page 16, lines 11 to 19 and at page 17, lines 16 to 18; support for Claim 55 is found at page 13, lines 31 to 32; and support for Claim 56 is found at page 17, lines 18 to 19. Support for Claim 57 can be found at page 26, line 28-page 27, line 19.

II. Substitute specification

As requested by the Examiner, Applicants respectfully submit a substitute specification under 37 CFR §1.125(a) complying with formal requirements. The specification is identical to the specification originally filed and thus, no new matter has been added. Since the only modification to the original specification are the margins and no changes to the text have been made, no marked up copy of the original specification is provided herewith.

III. Rejection of Claims 1-12 under 35 USC 112, 2nd paragraph

The Examiner rejected Claim 1 and the dependent Claims 2-12 under 35 U.S.C. §112, 2nd paragraph, as being indefinite with respect to the term "thermal transfer membrane" used in Claim 1.

Applicants respectfully note that Claim 1 recites a device containing not a thermal transfer membrane, but a thermal transfer member. Nevertheless, in order to more clearly point out the invention, Applications have amended Claims 1 and 12. Claims 1 and 12 now refer to a "temperature regulated zone" of the microfluidic substrate rather than to a "thermal transfer member". Support for a "temperature regulated zone" is found throughout the specification, including, among many places, at page 5, line 28, page 6, line 11, and page 6, line 30. A representative function of the temperature regulated zone is further provided in the specification at page 2, line 32 to page 3 line 1, wherein a zone of a channel corresponds to a step of a protocol

to be carried out in a microchannel. Further representative examples of zones capable of thermal cycling and examples of their implementation are found in the specification as noted above, and in the Examples, including in Example 1 at page 73, line 1 to page 73, line 13, and in Examples 5 and 6 at pages 78, line 18 to page 81, line 22.

Accordingly, withdrawal of the rejections of Claims 1-12 under 35 U.S.C. §112, 2nd paragraph, is respectfully requested.

IV. Rejection of Claims 1-12 under 35 U.S.C. §102

Claims 1-12 are rejected under 35 U.S.C. §102 as allegedly being anticipated by Wilding et al. (US Patent 5,726,026).

U.S. Patent 5,726,026 teaches flow miniaturized devices allowing preparation and various testing of biological samples. In particular, it discloses devices allowing nucleic acid amplification using thermocycling techniques. Such thermal amplification is carried out by submitting minute amounts of biological samples to different temperatures by two different means.

The first means involves transporting the sample into a single chamber (Fig 7, ref 127) wherein the temperature is cycling (*see*, columns 12 line 61 to column 13 line 25). In this reference, thermal amplification is carried out on a sample which is stationary in the amplification region and thus that is not continuously flowing as recited in Claim 1.

The second means involves moving the sample back and forth between two chambers set at two different temperatures (*see*, column 20 lines 28-36; Fig 11A, elements 198a and 198b). However, this device is also not designed to work in continuous flow as the fluid is moved back and forth between two different regions of the pathway during the thermal amplification and is not continuously flowing through the pathway. Hence, the amplification region has to be separated from the other regions and only one sample can be handled at a time in this nucleic acid amplification region.

Likewise, in the second means, the two chambers are each at a single constant temperature. Thus, in contrast to the present device, the second means does not contain a zone which cycles between at least two temperatures but rather contains two zones which are at static temperatures.

By contrast, in the present application, the claimed device permits thermal amplification on a sample that is continuously flowing along the nucleic acid amplification region. As stated in the description, devices of the invention allow all steps of a given process, including thermal amplification, to be operated while the sample is continuously flowing. Indeed, devices of the invention are designed so that the sample is adjusted to different temperatures while it is circulated within a given portion of the pathway. Thus, the flowing sample is brought successively to the different temperatures required by the thermal cycling while continuously flowing in the thermal amplification region. In one representative embodiment, the number of times that the sample undergoes thermal cycling may be determined by choosing the flow speed . (*see* specification, page 38, lines 27-29).

Therefore, Wilding et al. do not teach each essential limitations of the claimed invention, namely devices allowing thermal amplification on a sample that is continuously flowing along a portion of a sample pathway. Accordingly, Applicants respectfully request withdrawal of the rejections of Claims 1-12 under 35 U.S.C. §102.

V. Conclusion

In view of the foregoing, it is submitted that the pending Claims 1-12 and 52-56 are in condition for allowance. Reconsideration and withdrawal of the rejections is respectfully requested. Should the Examiner have any questions regarding this matter, he is urged to telephone the undersigned so that the question is resolved.

Please charge any additional fees, including any fees for additional extension of time, to Deposit Account No. 11-1410.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. A device comprising:

a microfluidic substrate comprising at least one pathway for sample flow; and

said microfluidic substrate further comprising at least one ~~thermal transfer member~~ temperature regulated zone which is capable of cycling between at least two temperatures, said at least one ~~thermal transfer member~~ temperature regulated zone being adapted to bring at least a portion of said sample pathway to said at least two temperatures while a sample is continuously flowing along said at least a portion of said sample pathway.

12. The device of Claim 1, wherein said ~~thermal transfer member~~ at least one temperature regulated zone comprises a metal bar in fluid communication with a plurality of water sources containing water at said at least two temperatures, said metal bar being in thermal communication with said at least a portion of said sample pathway.